

SHORT CASES IN CARDIOLOGY

Aortic stenosis in homozygous familial hypercholesterolaemia

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Homozygous familial hypercholesterolaemia (FH) is a rare disorder characterised by extreme hypercholesterolaemia, early appearance of cutaneous and tendon xanthomata, and premature cardiovascular involvement. Coronary artery disease (CAD) is common and is accompanied by aortic valve stenosis and atheromatous involvement of the aortic root. The surgical treatment of this condition carries a high risk even in skilled hands.

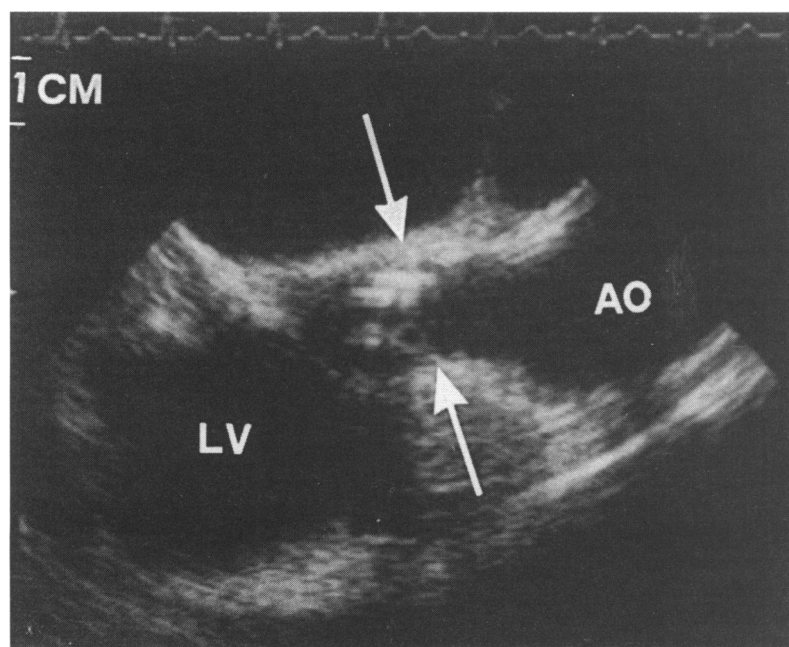
We report the case of a 25 year old Turkish woman who was referred with a presumptive diagnosis of homozygous FH; her only symptom was effort dyspnoea. On examination she had bilateral hemi-arcus, planar xanthomata in the webs of the fingers, and Achilles tendon xanthomata. Auscultation revealed a loud (4/6) ejection systolic murmur at the aortic area with a loud aortic closure sound.

She was taking daily doses of simvastatin (20 mg) and cholestyramine (12 g). Serum total cholesterol was 14.9 mmol/l, low density lipoprotein cholesterol (LDL) 13.7 mmol/l, triglyceride 0.94 mmol/l, high density lipoprotein cholesterol 0.88 mmol/l, and lipo-

protein (a) 23 mg/dl. An echocardiogram showed severe aortic stenosis with a mean gradient of 53 mm Hg. Eight months later she developed dizziness on exertion. Exercise echocardiography (modified Bruce) showed 3 mm down-sloping ST depression in inferolateral leads after 3 minutes, with extensive inferior akinesis. Repeat echocardiography with transoesophageal imaging showed that the diameter of the ascending aorta tapered down from 27 mm to 15 mm at the root (figure). The aortic sinuses were markedly thickened and echogenic, implying extensive atheromatous deposition. The aortic valve was also markedly thickened, mainly at the tips, but remained mobile. Cardiac catheterisation showed moderate stenosis of the left anterior descending coronary artery (LAD) and right ostial occlusion, a transaortic valvar gradient of 110 mm Hg, and funnelling of the aortic root with partial obliteration of the sinuses of Valsalva.

In view of her progressive symptoms and the severe aortic stenosis and CAD she underwent urgent cardiac surgery. The aortic valve, the cusps of which were thickened and had yellow deposits, was excised, the aortic root was enlarged with a pericardial patch and a 19 mm St Jude prosthesis was inserted. The left internal mammary artery was grafted to the LAD and the right internal mammary artery to the right coronary artery. Histological examination of the aortic valve showed focal deposition of cholesterol and calcium, together with fibrosis and chronic inflammatory changes.

Aortic root disease is the commonest cardiac manifestation of homozygous FH and by puberty all patients have some degree of atheromatous involvement of the ascending aorta. This results in ostial stenosis as atheroma in the sinuses of Valsalva encroaches on the coronary ostia, with a potentially fatal outcome. Although the supravalvar deposition of atheroma in itself is seldom haemodynamically important, it restricts full excursion of the aortic leaflets, creating secondary valvar aortic stenosis characterised by an ejection systolic murmur without a click and with a loud aortic closure sound.¹ The aortic valve itself is also infiltrated with atheroma but its mobility is relatively well preserved. The simplest way to monitor the severity of aortic stenosis is by Doppler echocardiography.²



Transoesophageal echocardiogram showing the characteristic tapering of the aortic root and sinuses owing to atheromatous infiltration of the proximal ascending aorta (arrows). Also note the thickened aortic cusps adding to the overall pressure drop. The mean transaortic gradient was 82 mm Hg.

Outcome in FH homozygotes undergoing aortic root reconstruction, insertion of prosthetic valve, and coronary artery bypass grafting at Hammersmith and St Mary's Hospitals, London

Case no	Sex	Age at operation	Operative procedure	Outcome
1	F	28	Björk-Shiley valve, ARR (Dacron graft), 3 grafts	Alive
2	M	19	Björk-Shiley valve, Konno operation, ⁴ 3 grafts	Died
3	M	31	Duromedics valve, ARR (pericardial patch), 3 grafts	Died
4	F	14	Björk-Shiley valve, ARR (pericardial patch), 1 graft	Alive
5	F	26	St Jude valve, ARR (pericardial patch), 2 grafts	Alive

ARR, aortic root reconstruction; CABG, coronary artery bypass graft.

The management of homozygous FH presents a major therapeutic challenge. The commonest form of lipid-lowering treatment nowadays is LDL apheresis every 1–2 weeks, usually combined with statins. This slows the rate of progression of aortocoronary atherosclerosis but can worsen the aortic stenosis because the removal of cholesterol may paradoxically accelerate valvar fibrosis.

Despite the improved prognosis resulting from medical treatment³ most patients eventually require surgery. The combination of severe aortic stenosis and CAD necessitates aortic valve replacement and coronary artery bypass grafting. Reconstruction of the aortic root is the main operative risk and carries a high mortality (table). In our patient (case 5) this procedure was successful, but two of four similarly treated patients died.

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